S1 SUPPORTING INFORMATION

The following search strings/criteria were used. Searches of reference lists were also undertaken for all relevant citations.

A. Search terms for search #1- studies describing the impact of OST on ART outcomes:
The following search string was used to search Medline, Global Health, EMBASE, Social Policy and Practice, the Cochrane library and Web of Science limited to references published between January 1, 1996 and June 15, 2014.
1."Methadone" or "Buprenorphine" or "Opioid-Related Disorders/drug therapy" or "Heroin Dependence/drug therapy" or "Morphine Dependence/drug therapy" or "Substance Abuse, Intravenous/drug therapy"
2. "HIV" or "human immunodeficiency virus" or "Acquired Immunodeficiency Syndrome" or "HIV/AIDS" or "HIV" or "AIDS" or "HIV-1"
3. "Anti-Retroviral Agents" OR "Anti-HIV Agents" OR "HIV Protease Inhibitors" OR "Antiretroviral Therapy, Highly Active/therapeutic use" OR "Antiretroviral Therapy, Highly Active/therapy"
1 AND 2 AND 3

B. Search terms for search #2- studies describing outcomes for PWID taking ART:
The following search terms were used to search between January 1, 1996 and November 30, 2014.
i. OVID platform- We used the Ovid platform to search Medline, EMBASE, PsychInfo, CAB and global health and Social Policy and Practice.

#	Searches
1.	exp HIV/ or exp HIV-1/
2.	human immunodeficiency virus.mp
3.	acquired immunodeficiency syndrome.mp or exp Acquired Immunodeficiency Syndrome/
4.	AIDS-related.mp or exp AIDS-related opportunistic infections/
5.	exp HIV infections/ or HIV infections.mp.
6.	1 or 2 or 3 or 4 or 5
7.	exp Antiviral agents/ or exp Anti-HIV agents/ or antiviral.mp. or anti-HIV.mp.
8.	exp Antiretroviral Therapy, Highly Active/ or antiretroviral.mp.
9.	exp HIV integrase inhibitors/ or exp HIV protease inhibitors/
10.	(Fosamprenavir or Atazanavir or Indinavir or Nelfinavir or Saquinavir or Ritonavir or Amprenavir or Darunavir or Lopinavir or ritonavir or kaletra or Tripanavir or tipranavir)
11.	nevirapine.mp. or exp Nevirapine/ or efavirenz.mp. or delavirdine.mp. or exp Delavirdine/
12.	(Abacavir or Stavudine or Didanosine or Lamivudine or Zidovudine or Zalcitabine or Combivir or Trizivir or tenofovir).mp. or exp Zidovudine/ or exp Lamivudine/
13.	reverse transcriptase inhibitors.mp. or exp Reverse Transcriptase Inhibitors/
14.	7 or 8 or 9 or 10 or 11 or 12 or 13
15.	exp Substance Abuse, Intravenous/
16.	((inject$ or intravenous) adj (drug$ or substanc$)).mp.
17.	((opiat$ or opioid$ or heroin$ or morphin$ or morfin$ or narcot$) adj2 (use$ or abus$ or misuse$ or addict$ or depend$)).ti,ab.
18.	exp opioid-related disorders/
19.	drug users.mp. or exp Drug Users/
20.	methadone.mp. or exp Methadone/ or methadone maintenance.mp
21.	exp opiate substitution treatment/
22.	buprenorphine.mp. or exp Buprenorphine/
23.	naltrexone.mp. or exp Naltrexone/
24.	(methadone or metadone or buprenor$ or LAAM or acetyl methadol or methadyl acetate or codein$ or morphin$).ti,ab.
25.	((substit$ or maint$) adj2 treatment)
26.	(substitution or maintenance).mp
27.	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
28.	6 and 14 and 27
29.	limit 28 to (adult or "300adulthood<age 18 years and older>")
30.	limit 29 to human
31.	limit 30 to yr="1996-Current"

32.	limit 31 to “review articles” [Medline]
33.	limit 31 to (meta analysis or “review”) [PsychInfo]
34.	31 not (32 or 33)
35.	“math$ model$”.mp
36.	34 and 35
37.	limit 34 to “cost-effect$”.mp
38.	34 not (35 or 37)

ii. **Web of Science, including Science and social science citation index: 1996-2014 (In topic)**
(HIV OR human immunodeficiency virus OR Acquired Immunodeficiency Syndrome OR HIV/AIDS OR HIV-1 OR HIV infections OR AIDS-related) AND (Opioid-Related Disorders OR Heroin Dependence OR Morphine Dependence OR Substance Abuse, Intravenous OR ((inject$ or intravenous) adj (drug$ or substanc$)) OR ((opiat$ or opioid$ or heroin$ or morphin$ or morfin$ or narcot$) adj (use$ or abus$ or misuse$ or addict$ or depend$)) OR drug user$ OR Methadone OR Buprenorphine OR Naltrexone OR opiate substitution treatment OR ((substit$ or maint$) adj (treatment)) OR metadone OR LAAM OR acetyl methadol OR methadyl acetate OR codein$) AND (Antiretroviral Agents OR antiretroviral therapy OR Anti-HIV OR HIV Protease Inhibitors OR antiretroviral OR reverse transcriptase inhibitors OR integrase inhibitors OR antiviral agents) NOT (meta-analysis OR review OR paediat$ OR pediatr$ OR “math$ model$” OR “cost-effect$” OR “in vitro” OR bioavailability OR “drug interactio$” OR “Phase I” OR pharmacokineti$ OR animal OR murine OR “HIV$ prevalence” OR “HIV$ incidence” OR “HIV$ transmission”)

iii. Cochrane CENTRAL registry of controlled trials- search strategy via Cochrane search interface
#1 HIV or "human immunodeficiency virus" or "Acquired Immunodeficiency Syndrome" or "HIV/AIDS" or "AIDS" or "HIV-1" or "HIV infection"

#2"Anti-Retroviral Agents" or "Anti-HIV Agents" or "HIV Protease Inhibitors" or "Antiretroviral Therapy, Highly Active/therapeutic use" or "Antiretroviral Therapy, Highly Active/therapy" or Fosamprenavir or Atazanavir or Indinavir or Nelfinavir or Saquinavir or Ritonavir or Amprenavir or Lopinavir or ritonavir or kaletra or Tripanavir or tipranavir or Protease inhibitors or Nevirapine or Delavirdine or Efavirenz or Abacavir or Stavudine or Didanosine or Lamivudine or Zidovudine or Zalcitabine or Combivir or Trizivir or Tenofovir or "reverse transcriptase inhibitors" or antiretroviral

#3 "substance abuse, intravenous" or opioid-related disorders or ((opiat$ or opioid$ or heroin$ or morphin$ or morfin$ or narcot$) adj (use$ or abus$ or misuse$ or addict$ or depend$)) or drug users or methadone or metadone or buprenor$ or naltrexone or LAAM or acetyl methadol or methadyl acetate or codein$ or "Methadone maintenance" or "Drug rehabilitation" or ((substit$ or maint$) adj treatment) or "opiate substitution treatment"

#4. #1 and #2 and #3

S2. STUDY METHODOLOGY

Statistical analysis

To provide a summary estimate for each outcome measure by OST status, reported crude odds ratios (OR) or hazard ratios (HR) and their corresponding standard error were log transformed. Adjusted estimates were also pooled and the effect size compared to the pooled crude estimate. Estimates of ART coverage, adherence, viral suppression, and attrition or treatment discontinuation, were pooled and results presented on the OR scale. Because one study reported a HR rather than an OR for attrition,[1] we derived an estimate of the OR by assuming an exponential distribution for the time to event.[2] Outcomes where the estimate of effect was predominantly reported as a HR to include follow-up time, namely mortality and ART uptake, were pooled and results presented on the hazard ratio (HR) scale. Two studies reported results for ART uptake as OR rather than HR.[3, 4] In one study,[3] it was possible to estimate the HR from the OR by assuming an exponential distribution for the time to event, but this was not possible for the other study[4] because there was insufficient

information.[2] Increases in CD4 counts were pooled using Standardised Mean Differences (SMD) using the Hedges g adjustment, to account for the large variation in scale of measurement across studies.[5] One study reported the OR for a "response" defined as an increase in CD4 cell count of 100.[6] This was converted to an SMD by assuming a logistic distribution for CD4 cell counts, so that the SMD was estimated by multiplying the log OR and its standard error by $\sqrt{3}/\pi$.[7]

Table S1. ART uptake outcomes

Cohort and Location	Study Reference	Recruitment site and method - inclusion criteria	Female population (%)	Intervention group	ART coverage or uptake % (n/N)	Comparison group	ART coverage or uptake % (n/N)	Effect Estimate (95%CI)
A. ART Coverage								
VIDUS- Vancouver, Canada	Strathdee et al., 1998/9[8, 9]	Self-referral, street outreach -Injected drugs in past month; resident in Vancouver region	39%	Enrolled in MMT	65% (26/40)*	Not enrolled in MMT	33% (45/137)*	OR=3.75 (1.77-7.97)
BHIVES- 10 sites USA	Altice et al, 2011 [3]	Provider referral, word of mouth, community outreach -Age>18, DSM-IV OD, excluded for alcohol or benzodiazepine abuse, mental illness or increased AST/ALT, pregnant	32%	BUP/NX for 4 quarters	65% (55/84)	BUP/NX for 1 quarter	53% (63/118)	OR=1.66 (0.93-2.94)
ALIVE- Baltimore, USA	Celentano et al, 1998[10]	Drug abuse treatment centers, STD & HIV clinics, parole officers, street outreach -Age>18, injected drugs between 1977 and study entry, CD4<500 in 1996	25%	On drug treatment	n/97[a]	Not on drug treatment	n/307[a]	aOR=2.12 (1.23-3.66)
New Jersey State, USA	Sambamoorthi et al., 2000[11]	Surveillance data of Medicaid records for PWID with drug abuse claims -Age>18, AIDS diagnosis; receiving Medicaid services for >90 days	28%	MMT >50% of time	87% (241/276)	Current drug abuse, based on ICD-9 CM codes	74% (615/833)	OR=2.13 (1.45-3.21)
New York State, USA	Turner et al., 2001[12]	Surveillance data of Medicaid records -Age>18, non-pregnant women with a live born delivery within 5 years	100%	Methadone treatment in previous 6 months	62% (159/255)	Illicit drug use in past 6 months	36% (56/157)	OR=2.99 (1.98-4.52)
INSPIRE- 5 cities, USA	Knowlton et al., 2010[13]	Community venues, shelters, medical clinics and methadone clinics -Injected drugs in past year, heterosexual act in past 3 months	38%	Current methadone treatment	60% (134/ 223)[c]	No current methadone treatment	50% (499/ 1002)[c]	OR=1.52 (1.13-2.04)
Amsterdam Cohort Studies on AIDS (ACSA)- Amsterdam, the Netherlands	Schinkel et al., 1998[14]	At methadone posts and STD clinics -PWID with CD4<500 starting PI-based ART	24%	In a methadone program	29% (28/97)	Not in a methadone program	17% (1/6)	OR=2.00 (0.20-18.20)
Barcelona, Spain	Vallecillo et al., 2010[15]	Referral to hospital detoxification units from outpatient clinics	25%	Methadone at admission	43% (164/380)	No methadone at admission	39% (113/293)	OR=1.21 (0.89-1.65)

Cohort and Location	Study Reference	Recruitment site and method - inclusion criteria	Female population (%)	Intervention group	ART coverage or uptake % (n/N)	Comparison group	ART coverage or uptake % (n/N)	Effect Estimate (95%CI)
		-Age>18, DSM IV OD with relapse or severe addiction						
Swiss HIV Cohort Study (SHCS)- Switzerland, Spain	Weber et al., 2009[4]	Referral from out-patient clinics of 7 hospitals -≥2 biannual cohort visits during study period and CD4 count and HIV-1 RNA measured at baseline visit	36%	OST in previous 6 months with and without current injecting drug use	47% (636/1348)	Injecting drug use in previous 6 months and no OST	33% (47/141)	OR=1.79 (1.24-2.57)
MANIF 2000-Marseilles, Nice and Paris, France	Escaffre et al., 2000[16]	Hospital clinic recruitment -Age>18, infected through injecting drug use	30%	In drug maintenance treatment in previous 6 months	40% (58/145)	Not in drug maintenance treatment in previous 6 months	49% (138/284)	OR=0.71 (0.47-1.06)
B. Recruitment onto ART								
BHIVES- 10 sites USA	Altice et al, 2011 [3]	Provider referral, word of mouth, community outreach -Age>18, DSM-IV OD, excluded for alcohol or benzodiazepine abuse, mental illness or increased AST/ALT, pregnant	32%	BUP/NX for 4 quarters	41% (26/64)	BUP/NX for 1 quarter	16% (9/55)	OR=3.46 (1.44-8.27)[d]
ALIVE- Baltimore, USA	Celentano et al, 2001[17]	Drug abuse treatment centers, STD & HIV clinics, parole officers, street outreach -Age>18, injected drugs within past 10 years	26%	MMT	81% (93/115)	Abstinence from injection drug use	70% (289/413)[c]	HR=1.68 (1.11-2.53)
ACCESS- Vancouver, Canada	Uhlmann et al., 2010[18]	Self-referral, street outreach -Injected drugs in past month; resident in Vancouver region	41%	Methadone use in previous 6 months	63% (35/55)[c]	No methadone use in previous 6 months	41% (72/176)[c]	HR=1.75 (1.26-2.43)
BART- Vancouver, Canada	Wood et al., 2005[19]	Self-referral, street outreach -Injected drugs in past month; resident in Vancouver region, never on ART at baseline	20%	On MMT at baseline	70% (119/171)	Not on MMT at baseline	44% (28/63)	aHR=2.10 (1.28-3.46)

ART, antiretroviral therapy; MMT, methadone maintenance treatment; DSM-IV OD, Criteria of Diagnostic and Statistical Manual of Mental Disorders, 4th Edition for opioid dependence; BUP/NX, buprenorphine naloxone drug maintenance treatment; OR, odds ratio; STD, sexually transmitted disease; aOR, adjusted odds ratio; MMT, methadone maintenance treatment; ICD-9-CM, International classification of diseases, 9th revision, Clinical modification; AST, aspartate aminotransferase or alanine transaminase levels; HR, hazard ratio; aHR, adjusted hazard ratio.

[a] Data not provided and unable to calculate from available data.

[b] N = HIV-infected PWID enrolled in care.

[c] estimated proportions from provided data

[d] estimate converted to a hazard ratio using available data

Table S2. Pooled estimates for the impact of opioid substitution therapy (OST) on ART outcomes

Outcome	Pooled estimate[a]	95% CI	I^2 test for heterogeneity	P for heterogeneity
Coverage of ART (*n*=10)	OR=1.54	1.17-2.03	67%	0.001
North America (*n*=6)	OR=1.84	1.40-2.43	37%	0.17
Europe (*n*=4)	OR=1.19	0.75-1.88	74%	0.14
Recruitment onto ART (*n*=4)	HR=1.87	1.50-2.33	0%	0.55
Adherence to ART (*n*=5)	OR=2.14	1.41-3.26	74%	0.004
Viral suppression (*n*=10)	OR=1.45	1.21-1.73	22%	0.24
ART discontinuation (*n*=7)	OR=0.77	0.63-0.95	59%	0.02
Mortality (*n*=6)	HR=0.91	0.65-1.25	74%	0.58
Asia (n=2)	HR=0.63	0.57-0.70	0%	0.74
North America and Europe (n=4)	HR=1.04	0.77-1.40	37%	0.19

[a] Calculated using random effects meta-analysis, OR=odds ratio, HR=hazard ratio, CI=confidence interval

Table S3. Adherence

Cohort and Location	Study Reference	Recruitment site and method - inclusion criteria	Female population (%)	Intervention group	Adherent % (n/N)[a]	Comparison group	Adherent % (n/N)[a]	Effect Estimate (95%CI)
VIDUS- Vancouver, Canada	Palepu et al., 2006[6]	Self-referral, street outreach -Age >18, illicit drug use in past month, reside in Vancouver region	42%	Enrolled in MMT in previous 6 months	n/161[b]	Not enrolled in MMT in previous 6 months	n/117[b]	OR=1.43 (1.11-1.84)
ACCESS- Vancouver, Canada	Tapp et al., 2011[20]	Self-referral, street outreach -Age >18, illicit drug use other than cannabinoids in past month	37%	Methadone treatment in previous 6 months	n/169[b]	No methadone treatment in previous 6 months	n/376[b]	OR=2.44 (2.01-2.96)
WIHS- 6 sites, USA	Kapadia et al., 2008[21]	Clinic referrals, community outreach, participant word of mouth -Women who had engaged in drug use at baseline or during follow-up on ART	100%	Medication based drug abuse treatment (methadone)	78% (58/74)	No drug abuse treatment	52% (32/62)	OR=3.40 (1.61-7.16)
Tartu, Estonia	Usukula et al., 2012[22]	Hospital clinic recruitment -Age>18, receiving ART	45%	Current opioid dependence treatment	85% (22/26)	No current opioid dependence treatment	85% (56/66)	OR=1.02 (0.23-4.44)
MANIF 2000-Marseilles, Nice and Paris, France	Moatti et al., 2000[23]	Hospital clinic recruitment -Age>18, infected through injecting drug use, CD4>300 in visit before enrolment, no OIs	32%	BUP in previous 6 months	78% (25/32)	No BUP in previous 6 months and active IDU	42% (8/19)	OR=4.91[c] (1.19-20.25)

ART, antiretroviral therapy; MMT, methadone maintenance treatment; IDU, injecting drug users; BUP, buprenorphine.
[a] N = HIV-infected PWID enrolled in care.
[b] Not presented in paper and OR is outcome of multivariate regression analysis.
[c] Calculated from provided data.

Table S4. Viral Suppression

Cohort and Location	Study Reference	Recruitment site and method - inclusion criteria	Female population (%)	Intervention group	Viral suppression % (n/N)[a]	Comparison group	Viral suppression % (n/N)[a]	Effect Estimate (95%CI)
VIDUS- Vancouver, Canada	Palepu et al., 2006[6]	Self-referral, street outreach -Age >18, illicit drug use in past month, reside in Vancouver region	42%	Enrolled in MMT in previous 6 months	n/161[b]	Not enrolled in MMT in previous 6 months	n/117[b]	OR=1.36 (1.07-1.72)
ACCESS- Vancouver, Canada	Ti et al., 2014[24]	Self-referral, street outreach -Age >18, Illicit drug use other than cannabinoids in past month	32%	Enrolled in MMT in previous 6 months	50% (106/211)	Not enrolled in MMT in previous 6 months	45% (169/376)	OR=2.14 (1.53-3.00)
Johns Hopkins HIV cohort- Baltimore, USA	Lucas et al., 2006[25]	Methadone clinics, HIV care provider referral -Age>18, baseline HIV-1 RNA>500 copies/ml, no triple-class drug resistance	35%	History of IDU, MMT at time ART initiated	32% (24/75)	History of IDU, no MMT at time of ART initiated	33% (81/244)	OR=0.95 (0.55-1.65)
ALIVE- Baltimore, USA	Westergaard et al., 2013[26]	Drug abuse treatment centers, STD & HIV clinics, parole officers, street outreach -Age>18, injected drugs between 1977 and study entry, attended ≥2 study visits	33%	Methadone treatment in previous 6 months	76% (125/165)	No methadone treatment in previous 6 months	69% (395/575)	OR=1.42 (0.95-2.11)
BHIVES- 10 sites USA	Altice et al, 2011[3]	Provider referral, word of mouth, community outreach -Age>18, DSM-IV OD, excluded for alcohol or benzodiazepine abuse, mental illness or increased AST/ALT, pregnant	32%	BUP/NX for 4 quarters	77% (65/84)[c]	BUP/NX for 1 quarter	72% (85/118)[c]	OR=1.32 (0.67-2.60)
Connecticut, USA	Springer et al., 2012[27]	Prisoners transitioning to the community -Age>18, DSM-IV OD, returning to New Haven or Hartford, not pregnant	19%	Any OST over 24 weeks	59% (35/59)[c]	No OST over 24 weeks	51% (18/35)[c]	OR=1.36 (0.59-3.15)
West Java, Indonesia	Achmad et al., 2009[28]	Hospital clinic recruitment -Age>18, ICD-9 OD in previous 12 months, attempt to stop opioids at least once	6%	Cases: All PWID enrolled in MMT	96% (24/25)	Control: Former PWID taking ART outside MMT clinic matched for date starting ART	90% (103/115)	OR=2.80 (0.35-22.59)
Madrid, Spain	Abellan et al., 1999[29]	NS -Starting PI-containing ART	25%	Methadone program at baseline	67% (12/18)	Active injecting drug user at baseline	50% (5/10)	OR=2.00 (0.41-9.71)
Swiss HIV Cohort Study (SHCS)- Switzerland	Weber et al., 2009[4]	Referral from out-patient clinics of 7 hospitals -≥2 biannual cohort visits during study period and CD4 count and	36%	OST in previous 6 months with and without current injecting drug use	74% (993/1348)	Injecting drug use in previous 6 months and no OST	71% (100/141)	OR=1.13 (0.77-1.66)

Cohort and Location	Study Reference	Recruitment site and method - inclusion criteria	Female population (%)	Intervention group	Viral suppression % (n/N)[a]	Comparison group	Viral suppression % (n/N)[a]	Effect Estimate (95%CI)
		HIV-1 RNA measured at baseline visit						
MANIF 2000-Marseilles, Nice and Paris, France	Roux et al., 2009[30]	Hospital clinic recruitment -Age>18, infected through injecting drug use, on ART for ≥6 months, OD during study	27%	OST in previous 6 months	75 % (75/100)[c]	No OST in previous 6 months	56% (18/32)[c]	OR=2.34 (1.11-4.93)

ART, antiretroviral therapy; MMT, methadone maintenance treatment; IDU, injecting drug use; PWID, people who inject drugs; ICD-9, International classification of diseases, 9th revision; DSM-IV OD, Criteria of Diagnostic and Statistical Manual of Mental Disorders, 4th Edition for OD, opioid dependence; OST, opioid substitution therapy (both methadone and buprenorphine); NS, not specified.

[a] N = HIV-infected PWID enrolled in care.

[b] Unable to calculate from available data.

[c] Calculated from provided data.

Table S5. CD4 Counts at or after ART Initiation

Cohort and Location	Study Reference	Outcome	Period	OST group	Estimate (IQR)	N
Madrid, Spain	Abellan et al., 1999[29]	Mean CD4 count gain	4 months after ART initiation[d]	MMT Active IDU	79 111	18 10
BHIVES- 10 sites USA	Altice et al., 2011[3]	Median CD4 count increase regression coefficient	12 months after ART initiation[d]	BUP 4 quarters BUP 1 quarter	46.3 (-19.9 – 112.4) 1	
Johns Hopkins HIV cohort- Baltimore, USA	Lucas et al., 2006[25]	Median CD4 count	ART initiation[d]	PWID-methadone PWID-nonmethadone	134 (IQR: 16-235) 125 (IQR: 26-240)	75 244
		Median CD4 count gain	6 months after ART initiation[d]	PWID-methadone PWID-nonmethadone	39 44	75 244
		Median CD4 count gain	12 months after ART initiation[d]	PWID-methadone PWID-nonmethadone	65 14	75 244
VIDUS- Vancouver, Canada	Palepu et al., 2006[6]	Proportion that gained 100 cells	58 months after ART initiation[d]	MMT Never MMT	OR=1.62 (1.3-1.72) OR=1.0	161 117

ART, antiretroviral therapy; MMT, methadone maintenance treatment; BUP, buprenorphine drug maintenance treatment; IDU, injecting drug use; PWID, people who inject drugs

[a]ART eligibility criteria ≤ 200 cells/mm^3.

[b]ART eligibility criteria ≤ 400 cells/mm^3.

[c]ART eligibility criteria ≤ 200 cells/mm^3 prior to 2008 and ≤ 350 cells/mm^3 from 2008.

[d] ART eligibility criteria not reported.

Table S6. Attrition on ART

Cohort and Location	Study Reference	Recruitment site and method - inclusion criteria	Female population (%)	Intervention group	ART or study discontinuation % (n/N)[a]	Comparison group	ART or study discontinuation % (n/N)[a]	Effect Estimate (95%CI)
VIDUS- Vancouver, Canada	Kerr et al., 2005[31]	Self-referral, street outreach -Age >18, illicit drug use in past month, reside in Vancouver region, had taken or were taking ART	43%	Methadone use in previous 6 months	39% (30/78)	No methadone use in previous 6 months	50% (41/82)	OR=0.62 (0.31-1.24)
ACCESS- Vancouver, Canada	Reddon et al., 2014[32]	Self-referral, street outreach -Age >18, illicit drug use other than cannabinoids in past month, on ART during study period	40%	Enrolled in MMT in previous 6 months	53% (111/210)	Not enrolled in MMT in previous 6 months	67% (133/198)	OR=0.52 (0.38-0.72)
ALIVE- Baltimore, USA	Kavasery et al., 2009[1]	Drug abuse treatment centres, STD & HIV clinics, parole officers, street outreach -Age>18, injected drugs between 1977 and study entry, free of AIDS at enrolment	28%	MMT in previous 6 months	49% (40/82)[b]	No MMT and no IDU in previous 6 months	50% (93/187)[b]	OR=0.96 (0.57-1.62)
INSPIRE- Baltimore, New York, Miami, San Francisco, USA	Knowlton et al., 2010[13]	Street-based, advertisement at shelters, AIDS service organisations, medical and methadone clinics -Injecting drug use in past year, sex with an opposite-sex partner in prior 3 months	38%	Current methadone treatment	30% (68/223)[b]	No current methadone treatment	40% (400/1002)[b]	OR=0.66 (0.49-0.89)
West Java, Indonesia	Achmad et al., 2009[28]	Hospital clinic recruitment -Age>18, ICD-9 OD in previous 12 months, attempt to stop opioids at least once	6%	Cases: All PWID enrolled in MMT	0% (0/35)	Control: Former IDU taking ART outside MMT clinic matched for date starting ART	3% (5/175)	OR=0.97 (0.38-2.51)
China	Zhao et al., 2013[33]	Enrollment in China's national ART program -Infected through injecting drug use and starting ART during the study period	12%	MMT at any time during study period	17% (892/5161)	No MMT at any time during study period	19% (3543/18652)	OR=0.89 (0.82-0.96)
Swiss HIV Cohort Study (SHCS)- Switzerland	Weber et al., 2009[4]	Referral from out-patient clinics of 7 hospitals -≥2 biannual cohort visits during study period and CD4 count and HIV-1 RNA measured at baseline visit	36%	OST in previous 6 months with and without current injecting drug use	27% (368/1348)	Injecting drug use in previous 6 months and no OST	27% (38/141)	OR=1.02 (0.69-1.50)

ART, antiretroviral therapy; OR, odds ratio; MMT, methadone maintenance treatment; STD, sexually transmitted disease; PWID, people who inject drugs; IDU, injecting drug use; ICD-9 OD, International classification of diseases, 9th revision opioid dependence; OST, opioid substitution therapy (both methadone and buprenorphine).

[a] N = HIV-infected PWID enrolled in care.

[b] Calculated from provided data.

Table S7. Mortality on ART outcome

Cohort and Location	Study Reference	Recruitment site and method - inclusion criteria	Female population (%)	Intervention group	Mortality % (n/N)[a]	Comparison group	Mortality % (n/N)[a]	Effect Estimate (95%CI)
ACCESS- Vancouver, Canada	Richardson et al., 2014[34]	Self-referral, street outreach -Age >18, Illicit drug use other than cannabinoids in past month	37%	Enrolled in MMT in previous 6 months	24% (47/194)	Not enrolled in MMT in previous 6 months	22% (147/666)	HR=0.87 (0.64-1.16)
ALIVE- Baltimore, USA	Vlahov et al., 2005[35]	Community outreach -Age>18, injected drugs between 1977 and study entry, ≥1 visit with CD4<200	27%	MMT in previous 6 months	1% (1/77)	No MMT in previous 6 months	2% (5/218)	HR=0.80 (0.46-1.39)
West Java, Indonesia	Achmad et al., 2009[28]	Hospital clinic recruitment -Age>18, ICD-9 OD in previous 12 months, attempt to stop opioids at least once in past	6%	Cases: All PWID enrolled in MMT	0.3% (1/35)	Control: Former IDU taking ART outside MMT clinic matched for date starting ART	1% (2/175)	HR=0.80 (0.20-3.20)
China	Zhao et al., 2013[33]	Enrollment in China's national ART program -Infected through injecting drug use and starting ART during the study period	12%	MMT at any time during study period	10% (538/5161)	No MMT at any time during study period	14% (2519/18652)	HR=0.63 (0.57-0.70)
Swiss HIV Cohort Study (SHCS)- Switzerland, Spain	Weber et al., 2009[4]	Referral from out-patient clinics of 7 hospitals -≥2 biannual cohort visits during study period and CD4 count and HIV-1 RNA measured at baseline visit	36%	OST in previous 6 months with and without current injecting drug use	20% (272/1348)	Injecting drug use in previous 6 months and no OST	15% (21/141)	HR=1.36 (0.87-2.12)
MANIF 2000- Marseilles, Nice and Paris, France	Michel et al., 2009[36]	Hospital clinic recruitment -Age>18, infected through injecting drug use	27%	OST in previous 6 months	n/100[b]	No OST, 92% heroin abstinent in previous 6 months	n/194[b]	HR=1.70 (0.72-4.01)

ART, antiretroviral therapy; MMT, methadone maintenance treatment; ICD-9, International classification of diseases, 9th revision; OD, opioid dependence; OST, opioid substitution therapy (both methadone and buprenorphine).

[a] N = HIV-infected PWID enrolled in care.

[b]Data not provided and unable to calculate from available data.

Table S8. Risk of bias in included studies using the Newcastle-Ottawa bias assessment tool

				Selection bias				Comparability	Outcome bias		
Author and year [ref]	**Cohort and setting**	**Type of sample**	**Outcomes**	**Representative-ness of exposed cohort**	**Selection of non-exposed cohort**	**Ascertainment of exposure**	**Outcome not present at study start**	**Comparability of cohorts**	**Outcome assessment**	**Duration of follow-up**	**Adequacy of follow-up**
Abellan 1999[29]	Madrid, Spain	HIV treatment cohort	VL	*	*	-	-	-	*	-	-
Achmad 2009[28]	West Java, Indonesia	OST and treat cohort	VL, LTFU, mort	-	-	*	VL/LTFU*; mort -	-	VL *; LTFU -; Mort *	VL *; LTFU *; Mort *	VL -; LTFU NA
Altice 2011[3]	10 sites, USA	HIV treatment cohort	VL, Rec, Cov	VL*; Rec/Cov-	*	*	VL *; recruit -; cov-	-	VL *; recruit -	*	-
Celentano 1998[10]	ALIVE, Baltimore, USA	PWID cohort	Cov	*	*	*	-	-	-	Cov NA	Cov NA
Celentano 2001[17]	ALIVE, Baltimore, USA	PWID cohort	Rec	*	*	*	*	-	-	*	*
Escaffre 2000[16]	MANIF 2000, France	PWID HIV cohort	Cov	-	*	*	-	-	*	Cov NA	Cov NA
Kapadia 2008[21]	WIHS, 6 sites, USA	Women's HIV cohort	Adh	*	*	*	-	*	-	Adh *	-
Kavasery 2009[1]	ALIVE, Baltimore, USA	PWID cohort	LTFU	*	*	*	*	-	*	*	NA
Kerr 2005[31]	VIDUS, Vancouver, Canada	PWID cohort	LTFU	*	*	*	*	*	*	*	LTFU NA
Knowlton 2010[13]	INSPIRE, 6 sites, USA	PWID community HIV cohort	LTFU, Cov	-	-	*	LTFU *; Cov -	-	-	LTFU *; Cov NA	LTFU NA; Cov NA
Lucas 2006[25]	Baltimore, USA	HIV treat trial in OST	VL	-	*	-	*	*	*	*	-
Michel 2009[36]	MANIF 2000, France	PWID HIV cohort	Mort	-	*	-	*	*	-	*	*
Moatti 2000[23]	MANIF 2000, France	PWID HIV cohort	Adh	-	*	*	-	*	-	*	*
Palepu 2006[6]	VIDUS, Vancouver, Canada	PWID cohort	Adh, VL	*	*	-	*	*	*	*	-
Reddon	ACCESS,	PWID	LTFU	*	*	*	-	*	*	*	NA

				Selection bias				Comparability	Outcome bias		
Author and year [ref]	**Cohort and setting**	**Type of sample**	**Outcomes**	**Representative-ness of exposed cohort**	**Selection of non-exposed cohort**	**Ascertainment of exposure**	**Outcome not present at study start**	**Comparability of cohorts**	**Outcome assessment**	**Duration of follow-up**	**Adequacy of follow-up**
2014[32]	Vancouver, Canada	community HIV cohort									
Richardson 2014[34]	ACCESS, Vancouver, Canada	PWID community HIV cohort	Mort	*	*	*	-	*	*	*	-
Roux 2009[30]	MANIF 2000, France	PWID HIV cohort	VL	-	*	*	*	*	*	*	
Sambamoor-thi 2000[11]	New Jersey, USA	Medicaid HIV cohort	Cov	*	*	*	-	-	*	NA	NA
Schinkel 1998[14]	ACSA, Amsterdam, Netherlands	HIV cohort	Cov	-	*	*	*	-	*	NA	NA
Springer 2012[27]	Conneticut, USA	Post-prison cohort of Dot ART	VL	-	*	*	*	*	*	-	*
Strathdee 1998/9[9]	VIDUS, Vancouver, Canada	PWID cohort	Cov	*	*	*	-	-	*	NA	NA
Tapp 2011[20]	ACCESS, Vancouver, Canada	PWID community HIV cohort	Adh	*	*	*	*	*	*	*	*
Ti 2014[24]	ACCESS, Vancouver, Canada	PWID community HIV cohort	VL	*	*	*	*	-	*	*	-
Turner 2001[12]	New York state, USA	HIV pregnant Medicaid women cohort	Cov	-	*	*	*	-	*	NA	NA
Uhlmann 2010[18]	ACCESS, Vancouver, Canada	PWID community HIV cohort	Rec	*	*	*	*	-	*	*	:*
Usukula 2012[22]	Tartu, Estonia	HIV treatment cohort	Adh	-	*	*	-	*	-	-	-
Vallecillo 2010[15]	Barcelona, Spain	PWID detoxification cohort	Cov	-	*	*	-	-	*	NA	NA
Vlahov 2005[35]	ALIVE, Baltimore mort	PWID cohort	Mort	*	*	*	-	*	*	*	-
Weber	Swiss cohort,	HIV treatment	LTFU, VL,	VL/Mort/LTFU*;	*	*	VL/Mort/	Mort *;	LTFU/mort-	VL/Mort/L	VL/Mort/

				Selection bias				Comparability	Outcome bias		
Author and year [ref]	**Cohort and setting**	**Type of sample**	**Outcomes**	**Representative-ness of exposed cohort**	**Selection of non-exposed cohort**	**Ascertainment of exposure**	**Outcome not present at study start**	**Comparability of cohorts**	**Outcome assessment**	**Duration of follow-up**	**Adequacy of follow-up**
2009[4]	Switzerland	cohort	Cov, Mort	Cov -			LTFU *; LTFU -	VL/LTFU/Cov -	VL/Cov *	TFU *; Cov NA	LTFU -; Cov NA
Westergaard 2013[26]	ALIVE, Baltimore, USA	PWID cohort	VL	*	*	*	-	-	*	*	*
Wood 2005[19]	BART Vancouver, Canada	PWID community HIV cohort	Rec	-	*	*	*	-	*	*	-
Zhao 2013[33]	China HIV treatment cohort	Nationwide HIV treatment cohort	LTFU, mort	*	*	Mort -; LTFU *	*	-	*	*	*

Scoring of each category was done using the Newcastle-Ottawa bias tool, available at http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. **Asterisks**=low risk of bias, **dashes**=high or unclear risk of bias, VL=viral load, LTFU=loss to follow up, Rec=recruitment, Cov=coverage, Adh=adherence, mort=mortality, NA denotes=not applicable. If a specific outcome is denoted next to an asterisk or dash then we decided that different outcomes had different risks of bias, whereas if just an asterisk or dash is shown then that applies to all outcomes of that study.

More details on risk of bias

Some studies had issues with respect to the representativeness of the cohort compared to community PWID. However, some were satisfactory if they assessed HIV treatment outcomes amongst a clinic sample of those on HIV treatment with or without OST. However, some studies suffered because they may not have had a representative sample of HIV infected PWID, with some recruiting from HIV outpatient clinics (MANIF 2000). With respect to the non-exposed cohort, most studies recruited them from the same cohort as those on OST, and so had a low risk of bias on this domain, and most determined if they were on OST by structured interview although some also linked to prescription databases. In contrast, some had issues with whether OST exposure occurred before the study outcome was recorded, with cohorts frequently recording exposure and outcome in the last follow up. The mortality outcomes were weakened on this domain because many did not assess whether the exposed had similar levels of HIV disease as those unexposed. Another weakness is that not all analyses adjusted for important cofounders or the outcomes used in the meta-analyses were not adjusted – however, when we undertook a sensitivity analysis to limit our analyses to adjusted estimates, our results did not substantially change. The outcome assessment was generally reported well with little risk of bias, except for attrition where only half of the studies could confirm the outcome through record linkage, and the adherence outcome where most studies relied on self-report (3/5) which can be prone to biases. Most studies did not have issues with length of follow up, but some had possible issues with attrition on different outcomes, with studies either not reporting it or having differential attrition amongst PWIDs but not controlling for it.

Table S9. Studies excluded due to presenting duplicate cohort data

Author and year [ref]	Study period[a]	Location- City, Country	Cohort or population[1]	Number on OST/Total (n/N)	Type of OST	Comparison population	Median follow-up (months)	ART outcomes in paper
Bassetti 1999[37]	1997	7 sites, Switzerland	SHCS – each participant in DMT in past 6 months presenting during a 2 month period	222/372	MMT	Active IDU	CS	Cov
Bouhnik 2002[38]	1997-1999	Marseilles, Nice and Paris, France	MANIF 2000 cohort- Infected through IDU	80/96	DMT	Active IDU	24	AD
Kerr 2004[39]	1996-	Vancouver, Canada	VIDUS cohort- PWID in past month recruited by self-referral and outreach	59/108	MMT	Active IDU	CS	AD
Krusi 2010[40]	1996-2007	Vancouver, Canada	Sister cohort to VIDUS- PWID in past month recruited by self-referral and outreach	157/381	MMT	Not on MMT-84% active IDU in past 6 months overall	30	VL AD
Mann 2012[41]	1996-2009	Vancouver, Canada	ACCESS cohort- illicit DU in past month recruited by self-referral and outreach	256/682	MMT	Not on MMT- 21% daily heroin injections overall	NA	AD
Milloy 2012[42]	1996-2009	Vancouver, Canada	ACCESS cohort- illicit DU in past month recruited by self-referral and outreach	NA/277	MMT	Not on MMT	32	VL AD
Nolan 2011[43]	1996-2008	Vancouver, Canada	ACCESS cohort- illicit DU in past month recruited by self-referral and outreach	NA/267	MMT	Not on MMT	51	VL
Palepu 2003[44]	1996-2001	Vancouver, Canada	VIDUS cohort- PWID in past month recruited by self-referral and outreach	54/234	MMT	Not on MMT-28% daily heroin injections overall	CS	VL
Palepu 2011[45]	1996-2008	Vancouver, Canada	ACCESS cohort- illicit DU in past month recruited by self-referral and outreach	169/545	MMT	Not on MMT – 28% daily heroin injections overall	24	AD
Pradier 2001[46]	1995-1998	Marseilles, Nice and Paris, France	MANIF 2000 cohort- Infected through IDU	26/33	DMT	Active IDU	10	VL
Sangsari 2012[47]	1996-2008	Vancouver, Canada	ACCESS cohort- illicit DU in past month recruited by self-referral and outreach	107/267	MMT	Not on MMT – 27% daily heroin injections overall	NA	VL
Westergaard 2011[48]	1998-2009	Baltimore, USA	ALIVE cohort- Active and former PWID, with ≥1 visit with viral suppression	71/437	MMT	Occasional or daily IDU	79	VL
Wood 2005[19]	1996-2003	Vancouver, Canada	BART cohort – PWID in past month recruited by self-referral and outreach	171/234	MMT	Not on MMT at baseline	24	UP
Wood 2006[49]	1996-2003	Vancouver, Canada	BART cohort – PWID in past month recruited by self-referral and outreach and who were unaware of their HIV status	NA/91	MMT	Not on MMT at baseline	24	UP

[1] illicit drug use includes all drugs except cannabinoids
SHCS, Swiss HIV Cohort Study; NA, not available; DMT, drug maintenance treatment including BUP and MMT; MMT, methadone maintenance therapy; BUP, buprenorphine maintenance therapy.
Note- Where there were multiple publications from the same study or cohort, we included the most comprehensive in the meta-analysis, as defined by number of participants, years covered, and comparability of outcome measure with other studies.

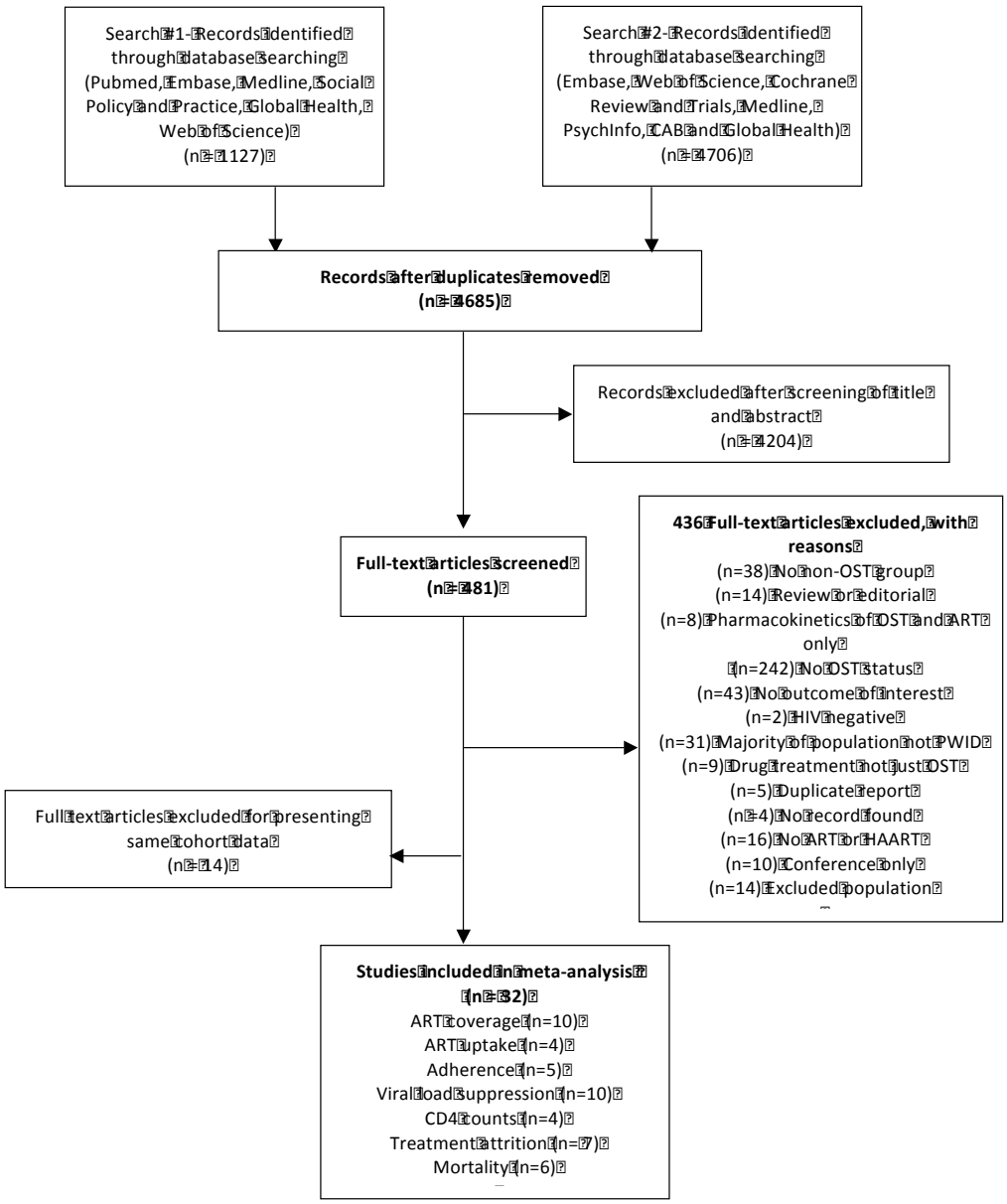

Figure S1. Flow chart of study selection for considering the impact of opioid substitution therapy on antiretroviral outcomes. OST= opioid substitution therapy, ART=antiretroviral therapy, HAART=highly active antiretroviral therapy.

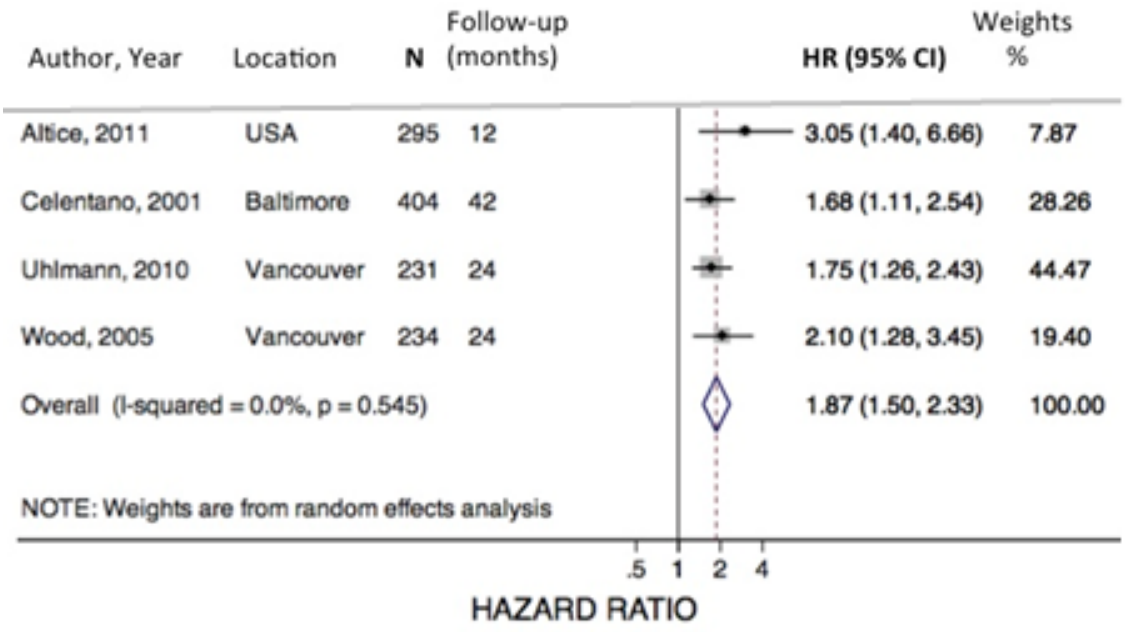

Figure S2. Forest plot of the effect of OST on recruitment onto ART among PWID, defined as the proportion of PWID who initiate ART over a given time period. I-squared and p-value are measures of between-study heterogeneity. N=total sample size of PWID**,** Follow-up=median participant follow-up duration, OR=odds ratio and CI=confidence interval.

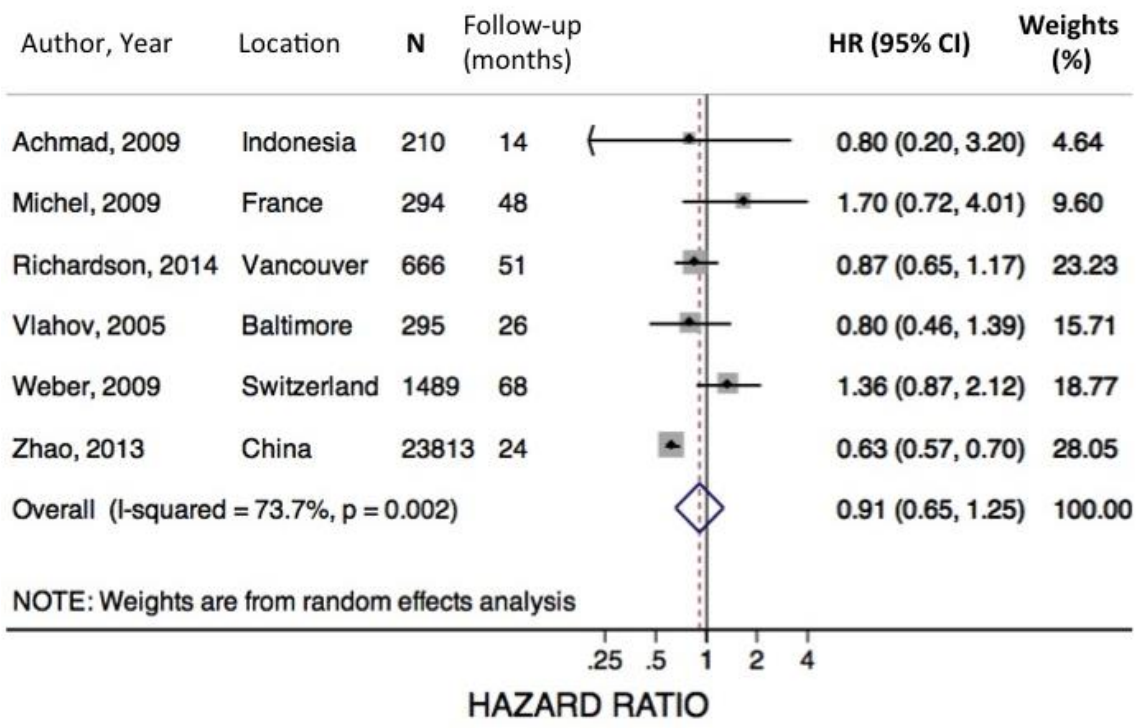

Figure S3. Forest plot of the effect of OST on mortality while on ART, defined as the proportion who died during follow-up due to HIV-related causes, or if this was not available, all-cause mortality. All studies described the effect of OST on all-cause mortality except for Vlahov who considered HIV-related mortality. I-squared and p-value are measures of between-study heterogeneity. N=total sample size of PWID, Follow-up=median participant follow-up duration, HR=hazard ratio and CI=confidence interval.

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